## *Remarks*

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 53-58, 60-77, and 79-93 are pending in the application. Claims 59 and 78 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Applicants retain the right to pursue the subject matter of the cancelled claims in one or more continuing applications. Support for the amendments can be found throughout the original claims and the specification. For example, support for the amendments to claims 53-58, 60-61, 63, 73-77, 79-80, and 82-87 can be found in the specification at page 3, line 30 to page 5, line 3. Support for the amendments to claims 64 and 93 can be found in the specification at page 3, line 30 to page 5, line 3; page 25, lines 10-12; and page 74, lines 9-10. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Applicants believe that entry of the amendments is proper because the amendments do not touch upon the merits of the application or are presented herein to advance the application in light of the Examiner's comments in the Office Action, dated December 4, 2002.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Claim Rejections Under 35 U.S.C. § 112, First Paragraph***

The Examiner has rejected claims 53-55, 57-63, 65, 66, 68, 71 and 72 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. (Paper No. 15, page 2.) Specifically, the Examiner has stated that the specification "does not reasonably provide enablement for *making* a nucleic acid molecule comprising a polynucleotide sequence that encodes a polypeptide having a first amino acid sequence that is less than 100% identical to the amino acid sequence set forth in SEQ ID NO:2 from positions 1 or 20 to position 182, wherein said polypeptide mediates apoptosis or inhibits tumor growth, or any polypeptide encoded by said nucleic acid molecule." (*Id.* at pages 2-3 (emphasis in original).)

The Examiner has also rejected claims 73, 76-83, 86-88 and 90-92 under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled by the specification. (Paper No. 15, page 3.) The Examiner is of the opinion that the specification "does not reasonably provide enablement for *making* a nucleic acid molecule comprising a polynucleotide sequence that encodes a polypeptide having a first amino acid sequence that is less than 100% identical to the amino acid sequence set forth in SEQ ID NO:4, wherein said polypeptide mediates apoptosis or inhibits tumor growth, or a polypeptide that is encoded by said nucleic acid molecule." (*Id.* (emphasis in original).) Applicants respectfully traverse the rejections.

In support of the rejection, the Examiner has stated that:

> the teachings of the specification cannot be extrapolated to the enablement of the claims because the specification does not teach one to *make* any nucleic acid molecule other than the one that encodes a protein having the amino acid sequence set forth in SEQ ID NO:2, which mediates apoptosis or inhibits tumor growth. While the specification teaches that a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID

> NO:2 can induce apoptosis or inhibit tumor growth, the specification does not teach how any other nucleic acid molecule can be produced that encodes a polypeptide that comprises an amino acid sequence that is *not* identical to the amino acid sequence set forth in SEQ ID NO:2, which is able to mediate apoptosis or inhibit tumor growth. Moreover, the specification does not teach which amino acid residues of SEQ ID NO:2 must be conserved, or which amino acids can be replaced, and by which other amino acids, within SEQ ID NO:2 so that a protein comprising a variation of SEQ ID NO:2 would also be capable of inducing cells to undergo apoptosis, or of slowing the growth rate of tumor cells. Therefore, because of the high level of unpredictability in the art, as established in the previous Office Action, one skilled in the art would not have a reasonable expectation of successfully producing any other species of the claimed genus of nucleic acid molecules, with the exception of the one comprising the polynucleotide sequence set forth in SEQ ID NO:1, without the need to perform additional, undue experimentation.

(*Id.* at pages 4-5 (emphasis in original).) The Examiner has also stated that "[b]ecause one would reasonably imagine that the claims encompass many non-working embodiments, which could not be identified by any means other than producing a species of polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:2 and determining whether or not the species induces apoptosis or inhibits tumor growth, finding the working embodiments among the possibilities would require undue experimentation." (*Id.* at page 9.) Applicants respectfully disagree with the Examiner.

Initially, Applicants note that contrary to the Examiner's suggestions, the claims do not encompass non-working embodiments. Because of the functional limitation recited in the claims, *i.e.*, "mediating apoptosis or inhibiting tumor growth," the claims encompass only working embodiments. Applicants submit that the full scope of the claims are enabled because it would not require undue experimentation to *make* nucleic acid molecules and polypeptides within the scope of the claims.

As Applicants have previously pointed out, the "message [for encoding proteins] is highly degenerate in that many different sequences can code for proteins with essentially the same structure and activity." Bowie *et al.*, *Science 257:*1306-1310 (1990). In addition, it is recognized in the art that "proteins are surprisingly tolerant of amino acid substitutions." *Id.* The Examiner has provided no evidence or line of reasoning to rebut these assertions. The Examiner has only stated that "the art lacks predictability." Applicants respectfully disagree. Because of the fact that many amino acid sequences can code for a protein with essentially the same structure and activity, one of ordinary skill in the art would expect that the vast majority of amino acid mutations would have little or no effect on the activity and structure of a given protein. Thus, although one of ordinary skill in the art would not be able to predict *with absolute certainty* that a given amino acid mutation (or mutations) would have little or no effect on the activity and structure of a given protein, one of ordinary skill in the art could *reasonably* expect that most mutations would *not* substantially alter protein function or structure. This is especially true given the knowledge in the art at the time of filing regarding conservative amino acid substitutions.

As the Examiner correctly notes, even a single amino acid substitution can in specific, particular instances affect the structure and activity of a protein. This is so because many proteins comprise critical residues which are essential for protein function. However, given that proteins comprise more than a single amino acid residue, the Examiner's observation does not speak to substitutions or mutations in the other plurality of amino acid residues which a protein comprises. *Not all amino acid residues in protein are critical to the activity of the protein.* This is why Bowie *et al.* concluded that proteins are "tolerant of amino acid substitutions." The reality is that the vast majority of amino acid residues within

a protein are not critical to structure and activity. Mutations at these residues will not alter the activity of a protein. Thus, the vast majority of amino acid substitutions (and other mutations) will not have a substantial effect on the activity and structure of a protein.

Once again, Applicants direct the Examiner's attention to the beta subunit of hemoglobin. It has been established that the majority of amino acid substitutions within the beta subunit of hemoglobin are functionally "silent." *See, e.g.,* Hutt *et al., Hemoglobin 20(4)*:371-6 (1996) (Exhibit A) ("Approximately 700 hemoglobin variants have been reported, causing a variety of clinical manifestations, with the majority being clinically silent."). Thus, Applicants assert that, in general, proteins are resilient to modification and retain functional activity notwithstanding numerous amino acid substitutions, deletions and insertions. Accordingly, the art is not as unpredictable as the Examiner suggests.

Moreover, the specification teaches assays which can be used to determine which variants of *tag7* fall within the scope of the claims, *i.e.*, are capable of mediating apoptosis or inhibiting tumor cell growth. *See* Specification, Examples 5-7, pages 67-70. Due to the high level of skill in the art of recombinant DNA technology and molecular biology, it would only be a matter of routine experimentation for one of ordinary skill in the art to make variants according to the methods described in the specification and to test them using the assays described in the specification to determine if they fall within the scope of the claims. Contrary to the Examiner's assertions, the level of experimentation would not be undue because all the methods used to generate variants and test for *tag7* activity are well-known and routine. The Examiner has proffered no evidence or line of reasoning that contradicts this.

The Examiner has, however, attempted to argue that the size of the genus somehow speaks the level of experimentation necessary to practice the invention. Specifically, the Examiner has stated that "as the specification does *not* teach how nucleic acid molecules that encode polypeptides that are less than 100% identical to SEQ ID NO:2 *that induce apoptosis or inhibit tumor growth* can be made, the artisan would be left to manufacture each and every species of nucleic acid molecule . . . and then determine whether the protein induces apoptosis or inhibits tumor growth." (Paper No. 15, page 9.) Moreover, the Examiner is of the opinion that "the claims would encompass a genus of roughly 7,300 members; but the present claims allow for a substitution, insertion, or deletion at any number of positions up to nine to be made . . . so the present claims may encompass a still vast genus of polypeptides." (*Id.*)

Irregardless of the size of the genus, Applicants need only show that it would not require undue experimentation to make a representative number of species within the genus to show enablement of the entire scope of the genus. *See Regents of University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998) (noting that a genus may be enabled by showing the enablement of a representative number of species within the genus); *see also In re Angstadt*, 537 F.2d 498, 502-03 (CCPA 1976) (deciding that applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art."). By generating variants using the methods described in the specification and testing the variants for activity using the assays described in the specification, a representative number of species within the genus can be made without undue experimentation. Thus, Applicants submit that the entire genus is enabled.

In support of this proposition, Applicants direct the Examiner's attention to Example 14 of the Synopsis of Application of Written Description Guidelines [hereinafter "Guidelines"]. The claim analyzed in Example 14 is substantially similar to Applicants' claims and recites:

> A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A—>B.

The hypothetical specification which supports this claim provides as follows:

> The specification exemplifies a protein isolated from liver and catalyzes the reaction of A—>B. The isolated protein was sequences and was determined to have the sequence as set forth in SEQ ID NO:3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. *The specifications indicates procedures for making proteins with substitutions, deletions, insertions and additions is routine and provides an assay for detecting the catalytic activity of the protein.*

(Emphasis added.)

Applicants' specification also teaches procedures for making variants of *tag7* and provides assays for detecting the activity of the protein. According to the Guidelines, the disclosure of Example 14 meets the requirements of 35 U.S.C. § 112, first paragraph, as providing adequate written description for the claimed invention. While Applicants are aware that there is a distinction between the written description requirement and the enablement requirement, Applicants submit that the hypothetical specification supporting the claim in Example 14 also meets the enablement requirement according to the USPTO guidelines. Otherwise, the Guidelines would be misleading to practitioners by showing an

example which meets the written description requirements only to fail on enablement grounds.

In view of the above, Applicants assert that claims directed to nucleic acid molecules encoding variants which are 95% identical to *tag7* which have *tag 7* activity and claims directed to polypeptide variants 95% identical to *tag7* which have *tag7* activity are enabled by the specification. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejections.

With particular respect to claims 64 and 93, the Examiner has stated that the specification "does not reasonably provide enablement for *making* any isolated naturally occurring nucleic acid molecule comprising a polynucleotide sequence that encodes amino acids 145 to 160 of SEQ ID NO:2 or any polypeptide comprising amino acids 145 to 160 of SEQ ID NO:2." (Paper No. 15, page 3 (emphasis in original).)

Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claims 64 and 93 so that they are directed to a "recombinant" nucleic acid molecule and a "recombinant" polypeptide. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

With respect to claims directed to polypeptides comprising amino acids 20 to 182 of SEQ ID NO:2, and nucleic acid molecules encoding said polypeptides, the Examiner has stated that "[w]hile it is plausible that a polypeptide comprising only the fragment of SEQ ID NO:2 spanning positions 20 to 182 might have an activity of a polypeptide comprising the full length amino acid sequence set forth in SEQ ID NO:2, given the high level of unpredictability in the art, one skilled in the art would not have a reasonable expectation of successfully producing a polypeptide comprising amino acids 20 to 182 of SEQ ID NO:2

that is capable of inducing apoptosis or inhibiting tumor growth without having to first perform additional, undue experimentation." (Paper No. 15, page 5.) Applicants respectfully disagree with the Examiner.

As taught by the specification, amino acids 20 to 182 of SEQ ID NO:2 correspond to the predicted mature form of the mouse *tag7* protein. (Specification, pages 15-16.) Polypeptides secreted by mammalian cells have a signal or secretory leader sequence which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. (*Id.*) Thus, since amino acids 20 to 182 of SEQ ID NO:2 represent the predicted cleaved form of *tag* 7, a polypeptide comprising said amino acids will very likely have the same activity as the uncleaved form of the polypeptide. Thus, one of ordinary skill in the art would not need to perform additional, undue experimentation to produce a protein comprising amino acids 120 to 182 which is capable of inducing apoptosis or inhibiting tumor growth. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also stated that "[a]s SEQ ID NO:4 is only marginally similar to SEQ ID NO:2, one skilled in the art would not have a reasonable expectation of successfully producing a polypeptide comprising amino acids 1 to 191 of SEQ ID NO:4 that is capable of inducing apoptosis or inhibiting tumor growth without having to first perform additional, undue experimentation." (Paper No. 15, page 5.) In support, the Examiner has stated that "one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, that the polypeptide of SEQ ID NO:4 is capable of inducing apoptosis or inhibiting tumor growth." (*Id.* at page 6.) Applicants respectfully disagree.

Contrary to the Examiner's contention, the state of the art shows that credible assertions of utility and function of a protein can be made based on homology studies. For example, Pawloski *et al.*, "Sensitive Sequence Comparison As Protein Function Predictor," *Pac. Symp Biocomput.* 42-53 (2000) (Exhibit B), teach that "the significance of the sequence similarity [between proteins] correlates well with the function similarity" and that the [e]xistence of even a very weak sequence similarity between two proteins increases the chance of them having similar function . . . ." (*Id.* at 11.) Other publications further confirm the value of homology studies in predicting protein function. *See, e.g.*, des Jardins *et al.*, *ISMB* 5:92-99 (1997) ("The most successful technique for identifying possible function of anonymous gene products . . . is performing similarity searches against sequence databases."); Holm, L., *Curr. Opin. Struct. Biol.* 8(3):372-79 (1998) (Exhibit C) ("By inferring homology between two proteins on the basis of sequence similarity, biologists can confidently predict that protein structure and function have remained similar during evolution."). Thus, given the fact that there is 77.2% similarity between SEQ ID NO:2 and SEQ ID NO:4, one of ordinary skill in the art would reasonably conclude that a protein comprising SEQ ID NO:4 would have the same activity as a protein comprising SEQ ID NO:2.

With respect to claim 57, the Examiner has stated that "although the amino acid sequence set forth in SEQ ID NO:1 encodes a murine, more specifically a mouse protein, the specification does not teach one to make any other nucleic acid molecule that encodes a murine protein." (Paper No. 15, page 6.) Applicants respectfully traverse the rejection.

Applicants believe that the rejection is directed to claim 59 (and not claim 57) as it recites the language that the Examiner objects. Solely to advance prosecution and not in

acquiescence to the Examiner's rejection, claim 59 has been cancelled. The Examiner's rejection is thus rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

With respect to claim 78, the Examiner has stated that "the specification does not teach one to make any other nucleic acid molecule that encodes a human protein." (Paper No. 15, page 6.) Solely to advance prosecution and not in acquiescence to the Examiner's rejection, claim 78 has been cancelled. The Examiner's rejection is thus rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also rejected claims 53-56, 59-63, 65, 66, and 68-70 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. (Paper No. 15, pages 9-10.) The Examiner has stated that the specification "does not reasonably provide enablement for *using* a nucleic acid molecule comprising a polynucleotide sequence that encodes a polypeptide having a first amino acid sequence that is less than 100% identical to the amino acid sequence set forth in SEQ ID NO:2 from positions 1 to 182 or at least 95% identical to the amino acid sequence set forth in SEQ ID NO:2 from positions 20 to 182, wherein said polypeptide could generate an antibody that specifically binds to a protein consisting of the amino acid sequence set forth in SEQ ID NO:2." (*Id.* at page 10.)

With respect to claims 73, 76-83, 86-88, and 90-92, the Examiner has stated that the specification "does not reasonably provide enablement for *using* a nucleic acid molecule comprising a polynucleotide sequence that encodes a polypeptide having a first amino acid sequence that is less than 100% identical to the amino acid sequence set forth in SEQ ID

NO:4, wherein said polypeptide mediates apoptosis or inhibits tumor growth." (*Id.* at page 10.) Applicants respectfully traverse the rejection.

While the basis of the Examiner's rejection is not clear, Applicants note that in view of the above comments regarding how to *make* the isolated nucleic acid molecules which encode polypeptides which mediate apoptosis or inhibit tumor growth and how to *make* isolated polypeptides which mediate apoptosis or inhibit tumor growth, one of ordinary skill in the art would not need to perform additional undue experimentation to proceed to *use* these nucleic acid molecules and polypeptides once made. For example, one of ordinary skill in the art could use the claimed nucleic acid molecules and polypeptides to mediate apoptosis and inhibit tumor growth. As demonstrated in Example 6, expression of *tag7* was shown to suppress the growth of VMR-0 cells *in vivo* in syngeneic mice. *Tag 7* polypeptides could be used, for example, to generate antibodies which bind *tag7* for use in diagnostic or purification applications. *See, e.g.* Example 14. In view of the Examples provided in the specification, it would not require undue experimentation to *use* nucleic acid molecules encoding polypeptides having *tag 7* activity and polypeptides having *tag 7* activity. Thus, the claims are enabled.

With respect to claims 64 and 93, the Examiner has stated that "it is apparent that a substantial number of members of the claimed genus of nucleic acid molecules and proteins will not bear any remarkable structural or functional homology to the polypeptide of SEQ ID NO:2." (Paper No. 15, pages 11-12.) Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claims 64 and 93 to recite "consisting essentially of" language. The Examiner has indicated that the specification is "enabling for a *using* a nucleic acid molecule comprising a polynucleotide sequence that

encodes a polypeptide consisting essentially of amino acids 145 to 160 of SEQ ID NO:2 ...." (*Id.*) Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner has also rejected claims 53-56, 59-67, 68, 70, 73, 75, 78-83, 85, 88 and 89 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention . . . ." (Paper No. 15, page 12.) Applicants respectfully traverse the rejection.

Specifically, the Examiner has stated that:

> Although the claims recite limitations requiring members of the claimed genus of polypeptides encoded by the claimed genus of nucleic acid molecules to be at least 95% identical to a reference amino acid sequence and to have the ability to either (a) generate an antibody that binds specifically to a protein consisting of said reference amino acid sequence, (b) induces apoptosis, or (c) inhibit tumor growth, if the members of the claimed genus of polypeptides do not induce apoptosis or inhibit tumor growth, but merely generate an antibody that binds specifically to a polypeptide consisting of said reference amino acid sequence, the written description would not reasonably convey to the skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed, or meet the requirements set forth under 35 U.S.C. § 112, first paragraph.

(Paper No. 15, page 13.) Based on these comments, it appears that the Examiner agrees that the requirements of 35 U.S.C. § 112, first paragraph, would be satisfied if the claims required that the polypeptides induce apoptosis or inhibit tumor growth. Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended the claims so that they no longer recite the limitation of generating an antibody specific to

*tag7*. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

As for claim 64, the Examiner has stated that it "encompasses a broad genus of nucleic acid molecules with widely varying attributes. . . . " (Paper No. 15, page 14.) Solely to advance prosecution and not in acquiescence to the Examiner's rejection, claim 64 has been amended to recite "consisting essentially of" language. Thus, the Examiners' rejection is rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

With respect to claims 59 and 78, the Examiner has stated that "the specification does not disclose any uniquely defining or identifying feature that is common among at least a substantial number of members of the claimed genera of nucleic acid molecules encoding murine and human polypeptides." (Paper No.15, page 15.) Applicants again note that these claims have been canceled in an effort to advance prosecution. Thus, the Examiner's rejection is rendered moot.

The Examiner has newly rejected claim 93 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (Paper No. 15, page 18.) Applicants respectfully traverse the rejection.

Specifically, the Examiner has stated that:

> [c]laim 93 recites the limitation "comprising amino acids 145 to 160 of SEQ ID NO:2." However, there does not appear to be proper and sufficient antecedent basis in the specification, including the original claims, for the recitation of this limitation in claim 93.

(*Id.*) Applicants respectfully disagree. Support for claim 93 can be found throughout the specification. For example, support can be found at page 23, lines 7-9. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

***Claim Rejections Under 35 U.S.C. § 102***

The Examiner has rejected claims 53-72 and 93 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kustikova *et al.*, *Genetika 32:*621 (1996) and Kustikova *et al.*, *Russian J. of Genetics 32:* 540546 (1996). (Paper No. 15, page 16.) Applicants respectfully traverse the rejection.

Applicants have provided herein an unexecuted Declaration of Dr. Sergei Kiselev Under 37 C.F.R. § 1.132.[1] In the Declaration, Dr. Kiselev, a co-inventor, states that the documents cited by the Examiner are the result of the his own work. Therefore, the two documents cited by the Examiner are not "by others." 35 U.S.C. § 102(a). In addition, Applicants have provided herein evidence that the actual publication date of the two documents was in fact in "late July" of 1996. (*See* Exhibit D.) As the instant application claims priority benefit to an application filed July 11, 1997, the two documents were not described in a printed publication "more than one year prior to the date of the application." 35 U.S.C. § 102(b). Thus, Applicants assert that the cited documents cannot properly be cited as 35 U.S.C. § 102 art. Applicants, therefore, respectfully request that the Examiner withdraw the rejection.

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[1] Applicants apologize for any inconvenience to the Examiner caused by filing an unexecuted Declaration. An executed Declaration will be filed shortly.

The Examiner has newly rejected claims 73, 75-77, 79-83 and 85-91 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kustikova *et al.*, *Genetika 32:*621 (1996) and Kustikova *et al.*, *Russian J. of Genetics 32:* 540546 (1996). (Paper No. 15, page 19.) Applicants respectfully traverse the rejection. As explained above, the documents cited by the Examiner cannot be properly cited as 35 U.S.C. § 102 art. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner also rejected claims 73, 75-77, 79-83 and 85-91 under 35 U.S.C. § 102(a) as allegedly being anticipated by Selsted (WO9729765-A1). (Paper No. 15, page 20.) Applicants respectfully traverse the rejection.

Applicants' own sequence alignment between SEQ ID NO:3 and nucleotide sequences encoding both the B-GPA and M-GPA proteins disclosed in Selsted revealed no more than 78% identity and 76% identity, respectively. (*See* Sequence Alignments, attached as Exhibit E). In addition, Applicants' own sequence alignment between SEQ ID NO:4 and the amino acid sequence of B-GPA and M-GPA revealed no more than 70% identity for both proteins. Thus, Selsted does not disclose the claimed invention. Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejection.

***Double Patenting Rejection***

The Examiner has rejected claims 53-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,172,211-B1. (Paper No. 15, page 21.) Applicants respectfully request that this rejection be held in abeyance until one or more claims of the captioned application are found

allowable. At that point, Applicants will file a terminal disclaimer in order to obviate the rejection or take other measures to overcome the rejection.

## *Conclusion*

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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